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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,532	01/25/2002	Jeffrey A. Lyon	003/240/SAP	2344

7590 05/26/2004

ATTN: MCMR-JA (Ms. Elizabeth Arwine-PATENT ATTY)
U. S. Army Medical Research and Materiel Command
504 Scott Street
Fort Detrick, MD 21702-5012

EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,532	LYON ET AL.	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The response to the First Action On Merits filed on 3/1/04 has been entered into the record.

Status of Claims

2. Claims 1, 3 and 5 have been amended.

Claims 1-11 pending in the application.

Specification Informalities maintained

3. Applicant states that the amendment to the specification will be made after receiving the ATCC depository information. Therefore, the objection of the disclosure for lack of complete information in the specification on page 6, ATCC address and plasmid pETATpfMSP-1_{42} (3D7) accession number is maintained.

Claim Rejections - 35 USC 112, first paragraph maintained

4. The rejection of claims 1-11 under 35 U.S.C. 112, first paragraph, as failing to provide an enabling disclosure without complete evidence that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of biological material, ATCC pETATpfMSP-1_{42} (3D7) is maintained for the same reason as stated above in paragraph # 3.

Claim Objection withdrawn

5. In view of amendment to claim 3, the objection for the abbreviation "MSP -1_{42}" is used without definition upon its first appearance in the claims is withdrawn.

Claim Objection maintained

6. The objection to the claim 3 for inducing an immune response against malaria infection and claim 5 for inducing a protective immune response to malaria is maintained as set forth in the previous office action.

Applicant requested the suggestions from the examiner to overcome the objection. Therefore, it is suggested claim 3 to rectie " A method for inducing a protective immune response against malaria infection - - - - - and E."

Claim 5 should be " a method for inducing an immune response to malaria in a - - - - - and E."

Claim Rejection - 35 USC § 103 maintained

7. The rejection of claims 1-11 under 35 U.S.C. 103(a) as being unpatentable over Kumar et al 1995, Molecular Medicine 1, 325-332 or Chang et al 1996, Infection and Immunity 64: 253-261 in view of Genton et al 2000, vaccine 18: 2504-2511. is maintained as set forth in the previous office action.

The claims are directed to a vaccine composition comprising P. falciparum MSP-1_{42} and an adjuvant selected from the group consisting of A, B, C, D and E, wherein said *P. falciparum* is 3D7 (claims 1-2). Claims are also drawn to method for inducing an immune response against malaria infection (claims 3-4) and a method of inducing protective immune response to malaria (claims 5-11) comprising administering a composition comprising. falciparum MSP-1_{42} and an adjuvant selected from the group consisting of A, B, C, D and E.

Kumar et al teach a vaccine composition comprising recombinant MSP-1_{42} from *P.falciparum*, FVO strain and Freund's adjuvant (see abstract). Kumar et al also teach a method of inducing an immune response to recombinant MSP- 1_{42} in Aotus monkeys by injecting recombinant protein in Freund's adjuvant (see page 327 lower right column). To determine whether the immunization with said protein induced an antibody response, sera from immunized animals were incubated with parasites (see page 328, lower left column and Table 1) in neutralization assays and inhibition of erythrocyte invasion was counted. Further, the prior art teaches a method for inducing protective immunity against malaria infection in Aotus Monkeys (see page 327, right column last paragraph) by injecting recombinant protein in adjuvant at multiple times. The immunized monkeys were challenged with *Plasmodium* parasites (page 328, upper left column). Immunized and control monkeys blood was collected and protective immunity was measured by estimating the percent parasitaemia (counting the parasites) in the blood.

Chang et al teach a vaccine composition comprising a recombinant baculovirus 42kD protein i.e., MSP-1_{42} (see abstract and page 254, left column, first paragraph under Materials and Methods) from *P.falciparum,* FUP strain and complete Freunds adjuvant. Further, to determine whether the immunization with said protein induced an immune response, sera from immunized monkeys were incubated with parasites (see page 254 Materials and Methods and Figure 1 and Table 2) in neutralization assays and inhibition of erythrocyte invasion was counted indicating that immunization with vaccine composition induced effective antibody response. Further, monkeys immunized with vaccine composition were protected against challenge infection. However, Kumar et al or Chang et al do not teach adjuvant selected from the group consisting of A, B, C, D and E and MSP-1_{42} is from P.falciparum 3D7.

Genton et al teach three component blood stage malaria vaccine including MSP 1 and MSP2 from *P.falciparum* 3D7 and an adjuvant ISA720 containing oil squalene, emulsifier from the mannide mono-oleate family, i.e., adjuvant B. This adjuvant has been shown to be safe and is used for human studies (see page 2505 under Materials and Methods) Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use protein from various strains including P.falciparum strain 3D7 (selecting a vaccine strain depends on the endemic area of the region) and adjuvant B in a vaccine composition, in a method of inducing an immune response or in a method of inducing protective immune response against malaria infection with a reasonable expectation of success because it would help in preparing a safe vaccine for human immunization for combating fatal malaria infection caused by *P.falciparum*. An artisan of ordinary skills would have been motivated to prepare MSP-1_{42} as taught by Kumar or Chang and combine with an adjuvant B as taught by Genton et al to a vaccine composition and use composition in a method of inducing an immune response or a method of inducing a protective immune response because the prior art suggests that the *P.falciparum* 3D7 is an effective vaccine candidate and adjuvant B is safe for human use (Genton et al) and Kumar et al or Chang et al teach recombinant MSP-1_{42} induces an effective immune response in Monkeys and protects monkeys against challenge infection. The claimed invention is a prima facie obvious over Kumar et al or Chang et al, each in view of Genton et al absent any convincing evidence to the contrary.

Applicant's arguments filed on 3/1/04 are fully considered but found to be non persuasive.

Applicant states that Kumar teaches E.coli GST-MSP 1_{42} fusion protein from Fvo strain of Falciparum and the presently claimed protein is from 3D7. Further applicant keeps on explaining to the examiner the differences (pages 5 and 6 of the response) between the claimed protein and the prior art protein.

The examiner understands the applicant's invention and the art used in the rejection. However, applicant's attention is drawn to claims 1, 3 and 5, which do not recite the limitation "strain 3D7". Therefore, it is the position of the examiner that the applicant has not provided any evidence to show that the claimed strain is different from the disclosed strain.

Applicant states that Genton et al teach adjuvant B in a malaria vaccine and does not disclose a vaccine comprising an MSP1_{42} protein that is expressed in a soluble protein from E.coli which retains its native folding and therefore, combining Kumar and Genton would not result in a vaccine comprising the fusion protein as claimed.

With respect to Chang et al, applicant states that the baculovirus recombinant polypeptide taught by Chang et al s from FVO isolate and does not disclose a vaccine comprising an MSP1-42 protein that is expressed in a soluble protein from E.coli which retains its native folding when combined with Genton et al.

The examiner disagrees with the applicant because applicant is arguing the limitation "3D7" that is not set forth in the claims 1, 3 and 5.

With respect to Genton et al, the claims are not rejected under 35 U.S.C. 102 but rejected under 35U.S.C.103 (a).

Please note the above rejection in which the examiner stated that " An artisan of ordinary skills would have been motivated to prepare MSP-1_{42} as taught by Kumar or Chang and combine with an adjuvant B as taught by Genton et al to a vaccine composition and use such composition in a method of inducing an immune response or a method of inducing a protective immune response because the prior art suggests that the *P.falciparum* 3D7 is an effective vaccine candidate and adjuvant B is safe for human use (Genton et al) and Kumar et al or Chang et al teach recombinant MSP-1_{42} induces an effective immune response in Monkeys and protects monkeys against challenge infection. The claimed invention is a prima facie obvious over Kumar et al or Chang et al, each in view of Genton et al absent any convincing evidence to the contrary " Thus, the examiner has established a clear prima facie obvious rejection over Kumar et al or Chang et al in view of Genton et al.

Finally, if the pETAT expression vector is critical to the claimed invention to obtain MSP1_{42} protein that could be recombinantly expressed in E.coli and results in a soluble protein, which retains its native folding, then the limitation "pETATpfMSP-1_{42} 3D7" should be set forth in the claims 1, 3 and 5. Applicant is encouraged to amend the claims 1, 3 and 5 to recite " pETATpfMSP-1_{42} 3D7" to overcome the rejection.

New Claim Rejections - 35 U.S. C. § 112, second paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 1-11 are rejected under 35 U.5.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3 and 5 are vague in reciting "as a soluble protein". Does applicant intend to mean the claim to read as " to produce a soluble protein?"

Remarks

10. No claims are allowed.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP ' 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

12. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D.

5/18/04

L. F. Smith

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